INTRODUCTION

Overview — The Health Consequences of Smoking

OVERVIEW – HEALTH CONSEQUENCES OF SMOKING

The statement, *"Warning: The Surgeon General Has Determined That Cigarette Smoking Is Dangerous to Your Health,"* has been required by law on cigarette packaging since 1970 as a part of the Public Health Cigarette Smoking Act of 1969. This Act was a response by the U.S. Congress to the scientific information on the health consequences of cigarette smoking summarized in reports then available (the Surgeon General's Report of 1964 and the subsequent 1967, 1968, and 1969 PHS Health Consequences of Smoking). This Act was passed because a series of important questions concerning cigarette smoking and health had been answered.

The following discussion summarizes the basic questions, the methodology used to determine the answers, and the answers themselves.

The initial question to be answered concerning the health consequences of smoking was *"Are there any harmful health effects of smoking cigarettes?"* The answer to this question was provided in two ways. First, it was demonstrated that some diseases occurred more frequently in smokers than in nonsmokers. Second, a causal relationship was established between smoking and these diseases.

Concern about the possible health effects of smoking started when scientists began looking for an explanation to account for the rapidly increasing death rate from lung cancer. The early retrospective studies showed a link between lung cancer and smoking. The first prospective studies, however, found that only one-eighth of the excess overall mortality found among smokers could be accounted for by lung cancer; the rest was largely due to coronary heart disease, chronic respiratory disease, and other forms of cancer. They also found that the effect on overall mortality was largely confined to cigarette smokers rather than the users of other forms of tobacco.

However, demonstrating an association by statistical probability is not enough to establish the causal nature of a relationship. Determining that the association between smoking and excess death rates is cause and effect was a judgment made after a number of criteria had been met, no one of which by itself is sufficient to make this judgment. These criteria as listed in the Surgeon General's

Advisory Committee Report (1964) were the **consistency, strength, specificity, temporal relationship,** and **coherence** of the association.

In addition, convincing theories about the mechanisms whereby smoking contributes to the various diseases responsible for the excess mortality among cigarette smokers were developed from the evidence on the biochemical, cytologic, pathologic, and pathophysiologic effects of cigarette smoking, thereby providing the necessary support for the decision that the relationship was causal.

The most important specific health consequence of cigarette smoking in terms of the number of people affected is the development of premature coronary heart disease (CHD). Both prospective and retrospective studies clearly established that cigarette smokers have a greater risk of death due to CHD and have a higher prevalence of CHD than nonsmokers. Long-term followup of healthy populations has confirmed that a cigarette smoker is more likely to have a myocardial infarction and to die from CHD than a nonsmoker. Cigarette smoking has been shown to be one of the major independent CHD risk factors and to act in combination with other major alterable CHD risk factors (high blood pressure and elevated serum cholesterol). Autopsy studies have shown that persons who smoked cigarettes have more severe coronary atherosclerosis than persons who did not smoke. Physiologic studies and animal experiments have indicated several mechanisms whereby these effects can take place.

A second major health consequence of smoking is the development of cancer in smokers. Cigarette smoking was firmly established as the major risk factor in lung cancer. The risk of developing lung cancer was found to be 10 times greater for cigarette smokers than for nonsmokers. The risk of developing lung cancer increases with the number of cigarettes smoked per day and is greater in cigarette smokers who report inhaling, who started smoking at an early age, or who have smoked for a greater number of years. Smokers of filter cigarettes have been shown to have a lower risk of developing lung cancer than smokers of nonfilter cigarettes, but the risk remains well above that for nonsmokers. The risk of developing cancer of the larynx, pharynx, oral cavity, esophagus, pancreas, and urinary bladder was also found to be significantly higher in cigarette smokers than in nonsmokers. Pipe and cigar smokers were found to have elevated risks for the development of cancer of the oral cavity, pharynx, larynx, and esophagus when compared to nonsmokers. Fewer pipe and cigar smokers than cigarette smokers report that they inhale. As a result lungs of pipe and cigar smokers receive much less

exposure to smoke than the lungs of cigarette smokers. This is probably the primary reason for the lower incidence of cancer of the lung for pipe and cigar smokers compared to cigarette smokers.

Women have had far lower rates of lung cancer than men. This has been attributed to the fact that fewer women than men smoke and the fact that women smokers generally select filter and low tar and nicotine cigarettes. However, the percentage of women smokers in the United States has increased steadily in the last 30 years, and since 1955 the death rates from lung cancer in women have increased proportionately more rapidly than the rates for men, reflecting this increased proportion of women smokers.

The tar from cigarette smoke has been found to induce malignant changes in the skin and respiratory tract of experimental animals, and a number of specific chemical compounds contained in cigarette smoke were established as potent carcinogens or co-carcinogens. Malignant changes including carcinoma *in situ* were found in the larynx and in the sputum exfoliative cytology of experimental animals exposed to cigarette smoke.

Nonmalignant respiratory disease is a third area of smoking-induced morbidity and mortality. Cigarette smokers have been shown to have more frequent minor respiratory infections, miss more days from work due to respiratory illness, and report symptoms of cough and sputum production more frequently than nonsmokers. Retrospective and prospective studies with long-term followup have found that cigarette smoking is the primary factor in the development of chronic bronchitis and emphysema in the United States. Cigarette smokers have also been found to be more likely to have abnormalities of pulmonary function and have higher death rates from respiratory diseases than nonsmokers. Data from autopsy studies have shown that cigarette smokers were more likely to have the macroscopic changes of emphysema, and that these changes are closely related to the number of cigarettes smoked per day. Mucous cell hyperplasia has been found more often in cigarette smokers. Cigarette smoke also inhibits the ciliary motion responsible for cleansing the respiratory tract.

An additional area of health concern has been the effect of cigarette smoking during pregnancy. Mothers who smoke cigarettes during the last two trimesters of their pregnancy have been found to have babies with a lower average birth weight than nonsmoking mothers. In addition cigarette smoking mothers had a higher risk of having a stillborn child, and their infants had higher late fetal and

neonatal death rates. There are some data to show that these risks due to cigarette smoking are even greater in women who have a high risk pregnancy for other reasons. These effects may occur because carbon monoxide passes freely across the placenta and is readily bound by fetal hemoglobin, thereby decreasing the oxygen carrying capacity of fetal blood.

Having established that cigarette smoking is a significant causal factor in a number of serious disease processes, two additional questions became important. They are *"Can the health consequences to the individual be averted by stopping smoking or by changing the cigarette,"* and *"What are the overall public health consequences of cessation and of the changes made in cigarettes?"*

The first question is the simpler of the two to answer. In the individual, cessation of cigarette smoking results in a rapid decline of the carbon monoxide level in the blood over the first 12 hours. Symptoms of cough, sputum production, and shortness of breath usually improve over the next few weeks. A woman who stops smoking by the fourth month of her pregnancy has no increased risk of stillbirth or perinatal death in her infant related to smoking. The deterioration in pulmonary function tests that occurs in some smokers becomes less rapid than that of continuing smokers. The death rates from ischemic heart disease, chronic bronchitis, and emphysema also become less than those of the continuing smoker. The risk of developing cancer of the lung, larynx, and oral cavity declines relative to the continuing smoker in the first few years after cessation and 10 to 15 years after stopping smoking approximates that of nonsmokers. A smoker who switches to filter cigarettes and has smoked them for 10 years or longer has a lower risk of developing lung cancer than a smoker who continues to smoke nonfilter cigarettes. The risk to a filter cigarette smoker, however, still remains well above that of a nonsmoker.

The public health benefits of cessation are more difficult to determine than the effects of cessation on the individual. Just as cause-specific death rates have reflected the effect of cigarette smoking on certain diseases, they should also reflect any substantial benefits to be gained by cessation or reduction in cigarette smoking. Several factors combined to produce a reduction in per capita dosage of tobacco exposure in the United States for the years 1966-1970. First, per capita consumption of cigarettes declined from 4,287 cigarettes per person in 1966 to 3,985 in 1970. Second, during this period there was a slow but significant decrease in the average tar and nicotine content of cigarettes as well as a decrease in the amount of

tobacco contained in the average cigarette. The decline in per capita consumption during those years occurred in the face of a substantial increase in the proportion of young women becoming smokers as compared to women of previous generations and so reflected predominantly a decrease in cigarette consumption by men.

Since 1970, although the per capita consumption of cigarettes has increased, the average levels of tar and nicotine have continued to decline, making it more difficult to predict what has happened to per capita dosage.

Examination of cause-specific death rates for the period of this declining per capita consumption reveals that there was a downturn in the male death rate from ischemic heart disease beginning in 1966 which reversed the upward trend that had occurred over the previous two decades. This decline in the death rate from ischemic heart disease has not occurred in women.

The male death rate from chronic bronchitis has also been declining since 1967, and the male death rate for emphysema has declined since 1968 when it was first recorded as a separate category. Female death rates for these two diseases have not shown these trends.

Despite the impressive coincidences of the decline in death rates among males occurring at the same time that there was a decline in per capita cigarette consumption, it is impossible to be certain of the exact cause of the decline in the death rates. These diseases are influenced by a variety of factors in addition to cigarette smoking such as blood pressure and air pollution. Some of these factors have also been subject to major control efforts which may have contributed to the decline in the death rates. In addition, there have been therapeutic advances in the treatment of these problems which may also have helped lower the death rates.

A decline in male death rates from lung cancer should also follow the decline in per capita consumption. This rate would not be influenced as much by changes in other etiologic factors or changes in therapy because cigarette smoking causes from 85 to 90 percent of all lung cancer and there have been no major improvments in survival due to changes in therapy. With lung cancer, however, two additional considerations must be kept in mind. A decline in death rates from lung cancer would be expected to lag several years behind a decline in per capita consumption. In addition, the decline in consumption and switch to low tar and nicotine cigarettes occurred

predominantly in the younger age groups where death rates from lung cancer are low. For these reasons, it is necessary to look at lung cancer death rates by age group rather than total lung cancer death rates. The lung cancer rates by age groups for 1971 suggest a decline in the lung cancer rates for the younger males (under 45), but the confidence limits on these trends at present remain wide enough that it is impossible to say whether this is a real decline or merely a leveling off. The national health statistics broken down by 5-year age groups are currently available only through 1971. The data by age group from a few more years will be necessary to determine whether the changes in smoking behavior which have taken place have reversed the trend of the preceding 40 years of continually increasing lung cancer rates in men. In 1971, the last year for which detailed mortality statistics are available, the accumulated exposure to cigarettes reached its peak among men born between 1915 and 1919, a group then in their early 50's. Cumulative exposure has continued to decline with each successive 5-year birth cohort born since then. The trends of the last few years offer some hope that the peak of the "lung cancer epidemic," as some have termed this phenomenon, may have been reached with this group and that future years will show a slow but consistent decline.

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Cardiovascular Diseases

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CORONARY HEART DISEASE (CHD)

Introduction

Coronary Heart Disease (CHD) is the most frequent cause of death in the United States and is the most important single cause of excess mortality among cigarette smokers. The evidence relating smoking to CHD has been reviewed in previous reports on the health consequences of smoking (*61, 62, 63, 64, 65, 66, 67, 68*). The following is a brief summary of the relationships between smoking and CHD presented in these reports.

Cigarette smoking, hypertension, and elevated serum cholesterol are the major alterable risk factors for myocardial infarction and death from CHD. Cigarette smoking acts both independently as a risk factor and synergistically with the other CHD risk factors. The magnitude of the risk increases directly with the amount smoked. The excess risk of CHD among smokers has been demonstrated in some Asian, Black, and Caucasian populations and is proportionately greater for younger men, especially those below age 50. Cessation of cigarette smoking results in a reduced mortality rate from CHD compared with the mortality rate for those who continue to smoke.

Pipe and cigar smokers have a slightly higher risk of death from CHD than nonsmokers, but they incur a much lower risk than cigarette smokers. This has been attributed to the lower levels of inhalation that characterize most pipe and cigar smoking.

Data from autopsy studies have shown coronary atherosclerosis to be more frequent and more extensive in cigarette smokers than in nonsmokers, and experimental work in humans and animals has suggested several mechanisms by which smoking may influence the development of atherosclerosis and CHD. The formation of carboxyhemoglobin, release of catecholamines, creation of an imbalance between myocardial oxygen supply and demand, and increased platelet adhesiveness leading to thrombus formation have all been demonstrated in smokers and proposed as explanations for the excess CHD mortality and morbidity among smokers.

Cigarette Smoking as a Major Risk Factor for Coronary Heart Disease

The evidence establishing smoking as a major risk factor in CHD has been reviewed in previous reports (*61, 62, 63, 64, 65, 66, 67, 68*). During the last year new epidemiologic data have been published on the relationship between coronary artery disease and smoking.

Bengtsson (*9, 10*) studied the smoking habits of women with myocardial infarction (MI) in Goteborg, Sweden. He found that smoking was significantly more common in a group of 46 women (80 percent smokers), ages 50-54, who had a myocardial infarction than in a control group of 578 healthy nonhospitalized women (37.2 percent smokers).

Other investigators examined the effect of cigarette smoking on survival of people with acute myocardial infarction. In a study of 400 patients with documented myocardial infarction who survived to be admitted to a coronary care unit, Helmers (*26, 27, 28*) found no significant difference between the percentages of smokers and nonsmokers among survivors studied after the first 24 hours, from 2 days until discharge, and from discharge to 3 years. Reynertson and Tzagournis (*52*), in a 5-year prospective study of 137 patients with documented CHD at age 50 or less, were also unable to find any relationship between CHD mortality rates and smoking habits. Smoking habits after entrance into the study were also considered and again no difference in mortality rates was found.

The Coronary Drug Project (*17*) found an effect of cigarette smoking on mortality after myocardial infarction. This group studied 2,789 men ages 30-64 years for 3 years after myocardial infarction and found a statistically significant correlation between cigarette smoking determined 3 months after a myocardial infarction and mortality (t-value of 2.94). None of these studies (*17, 26, 27, 28, 52*) were able to examine the smoking habits of the group of people who die suddenly as a first manifestation of CHD, and therefore may have excluded that group in which there is the highest excess mortality due to cigarette smoking (*31*).

Additional data from the Swedish twin study of Friberg, et al. (*23*) have been reported. They found an excess CHD mortality among smokers in dizygotic twins with different degrees of smoking, but no similar excess in monozygotic twins. Although the numbers were too small to be significant, the authors suggest that this tends to support the theory that both smoking and CHD are constitutionally

determined. These data must be viewed with caution, however, since the difference was demonstrable only in the older age group (born 1901 - 1910). When the younger age group (born 1911 - 1925) was considered, no excess CHD mortality was seen in the dizygotic group but a small excess was noted in the monozygotic group (three CHD deaths in the high smoking group and one in the low smoking group). Also the difference in cigarette consumption between the high and low smoking groups was relatively small (seven cigarettes per day). Consequently, data from this study are not sufficient to warrant the conclusion that both smoking and excess CHD mortality are constitutionally determined rather than smoking being a cause of the excess CHD mortality.

Cigarette Smoking in Relation to Other Risk Factors for Coronary Heart Disease

Cigarette smoking, elevated serum cholesterol, and elevated blood pressure are generally accepted as the three major modifiable risk factors for CHD. However, there is less agreement concerning other CHD risk factors – obesity, physical inactivity, diabetes mellitus, elevated resting heart rate, psychologic type A behavior, etc. The following studies present recent evidence on the relationships between smoking and hypertension, coffee drinking, and ventricular premature beats.

Hypertension

Results from several studies have shown that smokers on the average have slightly lower blood pressure than nonsmokers. Some investigators have attributed this finding to the fact that smokers on the average weigh slightly less than nonsmokers. Three current studies (*24, 36, 55*) discuss this relationship. Gyntelberg and Meyer (*24*), based on their evaluation of 5,249 men ages 40-59, were of the opinion that lower blood pressure in smokers could not be accounted for by differences in weight, age, or physical fitness. Kesteloot and Van Houte (*36*), in a study of 42,804 men, performed a multiple regression analysis on age, weight, and height and found that cigarette smokers had lower blood pressure than nonsmokers; however, when they included serum cholesterol values in the analysis, the difference in blood pressure was reduced to approximately 1 mm Hg. Although this difference was statistically significant based on the large population, the actual difference in blood pressure was too small to be of clinical importance.

Seltzer (*55*) studied 794 men selected for their initial good health and normal blood pressure (below 140 systolic and 90 diastolic) and followed them for changes in cigarette smoking habits, weight, and blood pressure. During the 5-year period of the study 104 men gave up smoking. For every age group except those over 55, there was a significantly greater weight gain (8 lb) among the "quitters" than among the continuing smokers (3.5 lb). Blood pressure increased 4 mm Hg systolic and 2.5 mm Hg diastolic in the quitters with no change in systolic and a slight reduction in diastolic (-1.1 mm Hg) in persons who continued to smoke. In order to examine blood pressure changes in relation to weight change, both continuing smokers and quitters were grouped according to their weight changes during the period of study (Table 1). The most significant finding was an increase in the systolic blood pressure (+1.77 mm Hg) among the quitters even in that group with significant weight loss. In contrast, the continuing smokers with significant weight loss had a decline in systolic blood pressure (-3.28 mm Hg). Diastolic blood pressure in quitters showed an increase with weight gain and no change with weight loss, while continuing smokers showed a decrease in diastolic pressure with weight loss and no change with weight gain. The data on subjects whose blood pressure had increased to hypertensive levels (systolic > 150 and diastolic > 95) were evaluated, and it was found that quitters had a much higher frequency of becoming hypertensive than continuing smokers (Table 2).

Seltzer, in interpreting these data, suggested that cigarette smoking tends to inhibit blood pressure increases, with only minimal pressure rises occurring even in instances of substantial weight gain. When this inhibiting effect of cigarette smoking is removed as in the case of the quitters, sharp rises in blood pressure become evident. He cautioned, however, that the development of hypertension in some quitters may have been responsible for decisions to lose weight and that his data do not allow an evaluation of the degree of blood pressure changes according to how recently cigarettes were given up.

The results of the ischemic heart disease study by Kahn, et al. (*34*) raise additional questions about Seltzer's data. Kahn followed 10,000 Israeli male civil service employees for 5 years to determine what factors were associated with an increased incidence of hypertension. He presented no data concerning persons who stopped smoking, but he did show that the incidence of hypertension increased with age and that the age-adjusted incidence of hypertension in smokers was over twice that of nonsmokers (76.9/1000 for smokers versus 35.4/1000 for nonsmokers). Seltzer reported no

TABLE 1. – *Age-standardized blood pressure changes (mm Hg)[1] at followup for continuing cigarette smokers and quitters according to weight changes*

Smoking Class	Weight Change (LB)							
	Significant Wt Loss		No Significant Wt Change		Moderate Wt Gain		Significant Wt Gain	
	No.	lb -25 to -5	No.	lb -4 to +4	No.	lb +5 to +12	No.	lb +13 to +30
Mean systolic BP changes:								
Continuing smokers	32	−4.00	84	−1.52	71	2.85	24	1.50
Quitters	13	1.77	27	2.22	27	4.04	32	3.69
Mean diastolic BP changes:								
Continuing smokers	32	−3.28	84	−2.04	71	0.73	24	−0.04
Quitters	13	−0.31	27	−1.96	27	4.30	32	3.94

[1] Standardized on basis of age distribution of current cigarette smokers.

Source: Seltzer, C.C. (*55*).

TABLE 2. – *Number of subjects who had developed hypertension at followup for continuing cigarette smokers and quitters*

Blood pressure levels	Continuing cigarette smokers		Quitters	
	Number	Percent	Number	Percent
Systolic blood pressure 150+	6	2.8	9	8.7
Systolic blood pressure 160+	2	0.9	5	4.8
Diastolic blood pressure 95+	3	1.4	5	4.8

Source: Seltzer, C.C. (*55*).

data on the incidence of hypertension in nonsmokers, and the age distribution for his group of smokers (the original source of the quitters) is heavily weighted toward younger age groups (with only 33 of 214 men age 50 years or over). According to Kahn's data, this age group would be expected to have a lower incidence of hypertension, and, in fact, Seltzer found only small numbers of men who developed hypertension (eight with diastolic hypertension) (Table 2). Making interpretations based on such small numbers is hazardous; for example, the difference between current smokers and quitters in the incidence of diastolic hypertension could have been produced by only three men quitting smoking because they developed hypertension.

Coffee Drinking

The Boston Collaborative Drug Study (*12*) recently reported a correlation between coffee drinking ($\geq$ 6 cups per day) and myocardial infarction that persisted after controlling for the effect of cigarette smoking. This was a retrospective study of 276 patients with a hospital discharge diagnosis of myocardial infarction and 1,104 age, sex, and hospital-matched controls discharged with other diagnoses. In addition to the usual limitations of retrospective studies, this study has several characteristics that make interpretation difficult. In controlling for the effect of cigarette smoking, the investigators divided the smokers into those who smoked one pack or less per day and those who smoked more than one pack per day. Because cigarette consumption is highly correlated with coffee consumption (*29, 39*), it can be expected that within such broad smoking categories those who were heavy coffee drinkers tended to be heavier smokers than those who consumed smaller amounts of coffee. It is also possible that the hospitalized controls represented persons who drank less coffee than the general population because of serious chronic illnesses. These characteristics of the study design do not allow firm conclusions to be made concerning the extent to which the relationship between coffee drinking and myocardial infarction is independent of the relationship of both variables to cigarette smoking.

The question of the independent nature of this relationship is also dealt with in a prospective study by Klatsky, et al. (*39*) of 464 patients with myocardial infarction who previously had had multiphasic health checkups. Both ordinary controls and CHD risk factor-matched controls were drawn from 250,000 people who had undergone the same multiphasic health checkups. The investigators did not find an independent correlation between coffee drinking and myocardial infarction when risk-matched controls were used.

The Framingham Study (*18*) recently published data on coffee drinking based on a 12-year followup of 5,209 men and women ages 30-62. An increased risk of death from all causes was demonstrated in coffee drinkers, but this relationship was accounted for by the association between coffee consumption and cigarette smoking. No association between coffee drinking and myocardial infarction or between coffee drinking and the development of CHD, stroke, or intermittent claudication was demonstrated. Heyden, et al. (*29*) also found no relationship between excessive coffee consumption (> 5 cups per day) and atherosclerotic vascular disease.

Ventricular Premature Beats

Ventricular premature beats have been shown to be a risk factor for sudden death from CHD. Vedin, et al. (*69*), in a study of 793 men in Goteborg, Sweden, examined the frequency of rhythm and conduction disturbances at rest and during exercise. They found no statistically significant correlation between cigarette smoking habits and the presence of supraventricular or ventricular premature beats at rest or during exercise.

CARBON MONOXIDE

Introduction

Carbon monoxide has long been recognized as a dangerous gas, but until recently concentrations which produced carboxyhemoglobin levels below 15 to 20 percent were thought to have little effect on humans. Currently there is considerable interest in determining the effect of chronic exposure to low levels of carbon monoxide (*65, 66, 67, 68*).

Carbon monoxide is present in concentrations of 1 to 5 percent of the gaseous phase of cigarette smoke (*11, 45*). The concentration varies with temperature of combustion as well as with factors which control the oxygen supply such as the porosity of the paper and packing of the tobacco. The amount of carbon monoxide produced increases as the cigarette burns down. Carboxyhemoglobin levels in smokers vary from 2 to 15 percent depending on the amount smoked, degree of inhalation, and the time elapsed since smoking the last cigarette.

Carbon monoxide, which has 230 times the affinity of oxygen for hemoglobin, impairs oxygen transportation in at least two ways:

First, it competes with oxygen for hemoglobin binding sites. Second, it increases the affinity of the remaining hemoglobin for oxygen, thereby requiring a larger gradient in Po_2 between the blood and tissue to deliver a given amount of oxygen; this increased gradient is usually produced by a lowering of the tissue Po_2.

Carbon monoxide also binds to other heme-containing pigments, most notably myoglobin, for which it has even a greater affinity than for hemoglobin under conditions of low Po_2. The significance of this binding is unclear, but may be important in tissues, such as the heart muscle, which have both high oxygen requirements and large amounts of myoglobin.

Sources of Carbon Monoxide Exposure and Human Absorption

Several researchers (*13, 32, 35, 57, 60, 70*) have estimated the relative contribution of cigarette smoking and air pollution to the human carbon monoxide burden as measured by carboxyhemoglobin levels (COHb). Kahn, et al. (*35*), in a study of 16,649 blood donors, determined that smoking was the most important contributing factor, followed by industrial work exposure. Nonsmoking industrial workers had COHb levels of 1.38 percent, and nonsmokers without industrial exposure had levels of .78 percent. Cigarette smokers, on the other hand, had very high levels. Smokers with industrial exposure had levels of 5.01 percent, while smokers without industrial exposure had levels of 4.44 percent (Tables 3 and 4). Stewart, et al. (*57*) found similar results in a nationwide survey of blood donors and noted marked variation in mean COHb levels in residents of different cities measured at different times of the year (Table 5). However, in all areas, smokers still had COHb levels two to three times higher than nonsmokers and had increasing COHb levels with increasing level of cigarette consumption (Table 6). Similar findings were reported by Torbati, et al (*60*) in a study of 500 male Israeli blood donors.

Nonsmoking workers exposed to automobile exhaust – London taxi drivers (*32*) and garage and service station operators (*13*) – have higher baseline levels of carboxyhemoglobin than nonsmokers of the general population. But even in these high exposure occupations smokers have markedly higher COHb levels (8.1 and 10.8 percent) than nonsmokers (6.3 and 5.5 percent). An extreme is represented by New York City tunnel workers who are exposed to an average of 63 ppm CO with peak exposure levels as high as 217 ppm CO; cigarette smokers still maintained much higher COHb levels (5.01 percent) than nonsmokers (2.93 percent) (*8*).

TABLE 3. – *Mean percent of carboxyhemoglobin saturation in smokers and nonsmokers by sex and race*

	Total Sample		Nonsmokers		Smokers[1]	
	No.	$\bar{X} \pm S_{\bar{X}}$	No.	$\bar{X} \pm S_{\bar{X}}$	No.	$\bar{X} \pm S_{\bar{X}}$
Total Sample	16,649	2.30 ± 0.02	10,157	0.85 ± 0.01	6,492	4.58 ± 0.03
Male	10,542	2.66 ± 0.03	5,888	1.00 ± 0.01	4,654	4.76 ± 0.04
Female	6,107	1.68 ± 0.03	4,269	0.64 ± 0.01	1,838	4.10 ± 0.06
White	15,167	2.28 ± 0.02	9,474	0.85 ± 0.01	5,693	4.66 ± 0.04
Male	9,669	2.65 ± 0.03	5,508	1.00 ± 0.01	4,161	4.83 ± 0.04
Female	5,498	1.63 ± 0.03	3,966	0.64 ± 0.01	1,532	4.19 ± 0.06
Black	1,429	2.59 ± 0.06	641	0.86 ± 0.03	788	4.00 ± 0.08
Male	829	2.91 ± 0.10	347	1.07 ± 0.05	482	4.24 ± 0.10
Female	600	2.15 ± 0.09	294	0.62 ± 0.04	306	3.63 ± 0.12

[1]Smokers are defined as those who smoked on the day of giving blood.

NOTE. – $\bar{X}$ = mean percent; $S_{\bar{X}}$ = standard error of mean percent.

Source: Kahn, A., et al. (*35*).

TABLE 4. – *Mean percent of carboxyhemoglobin saturation in smokers and nonsmokers by employment status*

	Nonsmokers		Smokers[1]	
	No.	$\bar{X} \pm S_{\bar{X}}$	No.	$\bar{X} \pm S_{\bar{X}}$
Persons employed	8,478	0.89 ± 0.01	5,962	4.61 ± 0.03
Classed as industrial workers[1]	1,523	1.38 ± 0.04	1,738	5.01 ± 0.06
Classed as workers other than industrial	6,955	0.78 ± 0.01	4,224	4.44 ± 0.04
Persons not employed	1,678	0.63 ± 0.02	531	4.24 ± 0.11

[1]Industrial workers are employed in either durable or nondurable goods manufacturing (craftsmen, operatives, or laborers). Smokers are defined as those who smoked on the day of giving blood.

NOTE. – $\bar{X}$ = mean percent; $S_{\bar{X}}$ = standard error of mean percent.

Source: Kahn, A., et al. (*35*).

TABLE 5. – *Median percent carboxyhemoglobin (COHb) saturation and 90 percent range for smokers and nonsmokers by location*

Location	Cigarette Smokers		Nonsmokers	
	Median	Range	Median	Range
Anchorage	4.7	0.9 – 9.5	1.5	0.6 – 3.2
Chicago	5.8	2.0 – 9.9	1.7	1.0 – 3.2
Denver	5.5	2.0 – 9.8	2.0	0.9 – 3.7
Detroit	5.6	1.6 – 10.4	1.6	0.7 – 2.7
Honolulu	4.9	1.6 – 9.0	1.4	0.7 – 2.5
Houston	3.2	1.0 – 7.8	1.2	0.6 – 3.5
Los Angeles	6.2	2.0 – 10.3	1.8	1.0 – 3.0
Miami	5.0	1.2 – 9.7	1.2	0.4 – 3.0
Milwaukee	4.2	1.0 – 8.9	1.2	0.5 – 2.5
New Orleans	5.5	2.0 – 9.6	1.6	1.0 – 3.0
New York	4.8	1.2 – 9.1	1.2	0.6 – 2.5
Phoenix	4.1	0.9 – 8.7	1.2	0.5 – 2.5
St. Louis	5.1	1.7 – 9.2	1.4	0.9 – 2.1
Salt Lake City	5.1	1.5 – 9.5	1.2	0.6 – 2.5
San Francisco	5.4	1.6 – 9.8	1.5	0.8 – 2.7
Seattle	5.7	1.7 – 9.6	1.5	0.8 – 2.7
Vermont, New Hampshire	4.8	1.4 – 9.0	1.2	0.8 – 2.1
Washington, DC	4.9	1.2 – 8.4	1.2	0.6 – 2.5

Source: Stewart, R.D., et al. (57).

TABLE 6. – *Mean percent carboxyhemoglobin (COHb) saturation in cigarette smokers 1 hour after last cigarette*

Location	Nonsmoker	Packs of Cigarettes Smoked Per day				
		< ½	½-1	1	1½	2
Milwaukee	1.3	3.0	4.2	5.3	6.2	4.7
New Hampshire, Vermont	1.4	3.3	4.4	5.7	6.7	5.3
New York City	1.4	3.1	4.3	4.7	5.8	6.3
Washington, DC	1.4	3.8	4.6	5.2	5.8	6.6
Los Angeles	2.0	4.0	5.2	6.0	7.4	7.5
Chicago	2.0	4.8	5.4	6.3	7.1	7.7

Source: Stewart, R.D., et al. (*57*).